VALIDITY OF MIDTRIMESTER SERUM BETA HCG IN PREDICTING PRE ECLAMPSIA IN HIGH RISK PREGNANCIES

Dissertation submitted to

THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY

in partial fulfilment for the award of the Degree of

M.D. OBSTETRICS AND GYNAECOLOGY

BRANCH II

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY

MADRAS MEDICAL COLLEGE

CHENNAI – 600 003

MARCH 2009

ACKNOWLEDGEMENT

I am extremely thankful to **Dr. T.P. KALANITI**, **M.D.,** DEAN, Madras Medical College and Government General Hospital, Chennai and **Dr. K. SARASWATHI M.D, DGO.,** Director and Superintendent, Institute of Obstetrics and Gynaecology, Egmore for granting me permission to utilize the facilities of the Institute for my study.

I am immensely grateful to our Director and Superintendent **Prof. Dr. K. SARASWATHI MD DGO.,** Institute of Obstetrics and Gynaecology, Egmore, Chennai, for her concern and support in conducting this study.

I am extremely thankful to our Deputy Superintendent, **Prof. Dr. T.K. RENUKA DEVI**, **MD, DGO.,** for her support in conducting this study.

I am thankful to **Prof.Dr. K. SARASWATHI M.D, DGO.,** Director and Superintendent, Institute of Obstetrics and Gynaecology, Egmore who is my guide in conducting this study.

I am thankful to the RMO and all UNIT CHIEFS for their support, advice and encouragement.

I am thankful to all Assistant Professors and Teachers for their guidance and help. I am thankful to all my colleagues for the help rendered in carrying out this dissertation.

I am thankful to **Dr. Padmanaban,** (Statistician) for his help in analysis of data.

Last, but not the least, I thank all my patients for their kind co-operation who made this study feasible.

CERTIFICATE

This is to certify that the dissertation entitled, **"VALIDITY OF MIDTRIMESTER SERUM BETA HCG IN PREDICTING PRE ECLAMPSIA IN HIGH RISK PREGNANCIES"** submitted by **Dr. R. RAMYA,** in partial fulfillment for the award of the degree of Doctor of Medicine in Obstetrics and Gynaecology by the Tamil Nadu Dr. M.G.R. Medical University, Chennai is a bonafide record of the work done by her in the Department of Obstetrics and Gynaecology, Madras Medical College, during the academic year 2006-2009.

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ETHICAL COMMITTEE CERTIFICATE

DATED : 25/2/08

I, Dr. R.RAMYA apply for the ethical committee certificate for the project **"VALIDITY OF MIDTRIMESTER SERUM BETA HCG IN PREDICTING PRE-ECLAMPSIA IN HIGH RISK PREGNANCY".** Under the guidance of Dr . K.Saraswathy,M.D. D.G.O., Director ,Institute of Obstetrics and Gynaecology ,Egmore Chennai-8.

I understand the implications of doing research with human subjects and will fully comply with the regulations and keep the dignity and protect the health of subjects at all costs.

R.Ramya.

SIGNATURE OF THE POSTGRADUATE STUDENT

I have no objection to guiding this postgraduate student in the project mentioned above.I Shall supervise to the extent that all the human rights are protected and research is carried on with utmost humanitarian principles.

K.Saraswathy

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SEAL OF GUIDE

I Certify that this project has been presented in front of the Ethical Committee , duly formatted in this institution and that all the members of the ethical committee have given
permission to conduct this research.

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CONTENTS

INTRODUCTION

Preeclampsia is a multisystem disorder of pregnancy and puerperium of unknown aetiology and characterised by Hypertension and Proteinuria. It is one of the major causes of maternal and perinatal mortality and morbidity. It complicates 5 – 8% of pregnancies.

The underlying pathophysiological mechanisms responsible for the disease process seem to appear between 8 and 18 weeks of gestation (**Robertson & Khong**, 1991). But the signs and symptoms become apparent in relatively late stages of pregnancy. So it is logical to search for predictive indicators.

Measurement in early pregnancy of a variety of biological, biochemical and biophysical markers implicated in pathophysiology of preeclampsia has been proposed to predict its development. Investigators have attempted to identify early markers of faulty placentation, reduced placental perfusion, endothelial cell dysfunction and activation of coagulation system. Attempts thus far have resulted in testing strategies with poor sensitivity and poor positive predictive value for preeclampsia. Currently there are no screening tests for preeclampsia that are reliable, valid and economical.

Some of the proposed predictive tests are:

1. **Haemodynamic tests**

a) *Angiotensin II infusion test* – Talledo et al**.** 1968.

By this test, abnormal vascular reactivity of patients destined to develop preeclampsia may be detected several weeks before clinical signs and symptoms appear. This test is done between 28 – 30 weeks. An increase in the diastolic BP more than 20 mm Hg during an Angiotensin infusion of 8 ng/ Kg or less predicts preeclampsia with a sensitivity of 90%, specificity of 87%, positive predictive value of 78% in high risk population, whereas those requiring more than 8 ng/Kg remain normotensive in 90%.

b) *Isometric hand grip test* – **Dagani et al**. Suggested a threshold increase of 20 mm Hg in diastolic BP when patients compresses inflated sphygmomanometer cuff for a 3 min time. Sensitivity of this test is 81%, specificity 96%, positive predictive value 81%. This test is done between 28 -32 weeks of gestation.

c) *Rollover test* – This test is proposed by Grant et al. This test is done between 28 – 32 weeks of pregnancy. Blood pressure is first recorded with the patient in left lateral position. An increase in diastolic BP of more than 20 mm Hg when the patient lies on the supine position is regarded as positive test. Sensitivity varies from 0-88%, specificity 5 -95%, positive predictive value 0-93%. This test is of no clinical use due to gross variation in results.

d) *Mean Arterial Pressure* – Page and Christianson suggested that patients with Mean Arterial Pressure more than 90 mm Hg in second trimester are at high risk for preeclampsia. But predictive values vary greatly.

2. **Doppler USG:** Campbell and associates reported that Doppler velocimetry of uterine umbilical vessels can predict preeclampsia as early as 18 weeks. Patients with preeclampsia had a characteristic notching of diastolic waveform, suggesting increased peripheral resistance due to impaired trophoblastic invasion of spiral arteries. Doppler may be useful to monitor the course of hypertensive disorders of pregnancy and the treatment effect, but it is not useful for screening pregnant women at low risk. Bower and colleagues 1993, used a two step screening test beginning at 18 – 20 weeks and its sensitivity for prediction of preeclampsia was 78% but positive predictive value was only 28%.

3. URINARY ASSAYS :

a) Urinary calcium excretion

b) Urinary calcium / creatinine ratio

c) Microalbuminuria

d) Urine Kallikrien / Creatinine ratio

e) Fasting urine albumin / creatinine ratio

4. MARKERS OF ENDOTHELIAL DYSFUNCTION:

a) Serum Fibronectin

b) Plasminogen activator inhibitors, cell adhesion molecules, serum thrombomodulin, endothelin 1.

c) Coagulation factors and Platelets

d) Serum uric acid

e) Others – atrial natriuretic peptide, haematocrit

Placental functional changes in the form of increased serum βhCG(Human chorionic gonadotrophin) have been documented and several prospective studies indicate changes in the hormone which can be detected before the clinical diagnosis of preeclampsia. Several investigators have found that an elevated level of serum βhCG in early second trimester is a useful predictor of preeclampsia.

REVIEW OF LITERATURE

Preeclampsia and eclampsia remain a difficult puzzle to solve. **Zweifel** and later **Chesley** called it a disease of theories. Probably the oldest reference was in the Athvaida Veda, 200 BC. **Mauriceau** in 1668 stated that primigravidas were at a greater risk for convulsions than multigravidas. **Demanent,** 1797 suggested oedema as a cause of convulsions in pregnancy.

Discovery of Proteinuria in preeclampsia was made by **Lever** and **Simpson** in 1843. In 1851, **Frerichs** published his work that eclampsia was a form of Uraemia. **Fishberg,** 1899 regarded preeclampsia as a cause of essential hypertension.

Discovery of hypertension as a cause for eclampsia was restricted to **Vaquez** and **Nabecourt** in 1897. **Bassier** (1790) first introduced the term "eclampsia**". De savages** (1739), had differentiated convulsions of eclampsia from epilepsy.

Castelli (1682), in his *Lexicon medium*, defined eclampsia as brightness lightning or **shining of froth as in a flashing glance.**

Emma J Davidson, Simon C et al conducted retrospective study in a group of 225 pregnant women who had PIH at term gestation. Their serum samples were tested at 15 – 20 weeks for βhCG, activin, inhibin, alpha fetoprotein as predictors of PIH. Of 225 women who had PIH at term, 24% of them had increased levels of βhCG at second

trimester.

Pankaj Desai, Sonal Rao et al conducted a study to find out whether βhCG can predict preeclampsia. Maternal serum βhCG at mid trimester was considered raised if levels were more than 2 multiples of median (MOM). 220 subjects were enrolled for the study. They were completely followed up. The study was carried out between 1995 – 2000, over a period of five years. There were 90 mothers with serum βhCG levels more than 2 MOM and 130 mothers with less than 2 MOM. 62 of 90 subjects with values of βhCG more than 2 MOM(68.9%) developed PIH against 21 of 130 (16.15%) with the βhCG less than 2 MOM. 59 out of 62 who developed PIH between 28 – 32 weeks had βhCG values more than 2 MOM. On the other hand 18 of 21 (85.71%) patients who developed PIH with βhCG less than 2 MOM did at after 32 weeks. In this study it was found that βhCG was the most efficient in predicting preeclampsia remote from term.

Tanya K Sorenson M.D.et al conducted a cohort study between 1990-1991. In this study, 180 women had elevated βhCG more than 2 MOM, 369 women had βhCG of less than 2 MOM. In 180 women who had βhCG more than 2 MOM, 71 women developed PIH with Proteinuria. The conclusion was that that the patients with increased βhCG values were at increased risk for preeclampsia (risk ratio 1.7, 95%, confidence interval 1.2-1.4).

Jaiswar S P, Nisha et al did serum βhCG estimation by enzyme immuno-assay in 162 pregnant women between 13-20 weeks of gestation. Of 162 women, 18 developed PIH. Those who developed PIH had serum βhCG ≥ 5000 µU / ml while 50% of those had serum βhCG more than 7000 µU/ml. Of 144 patients who remained normotensive, 99.3% had βhCG less than 4000 µ U/ml, while 74.21% had βhCG levels between 2000 to 3000 µU /ml.

R E Liepman, Williams et al conducted a cohort study of 460 women between Jan, 1990 and Aug, 1991. 460 women were subjected for triple screen analysis (Maternal serum alpha fetoprotein, βhCG and unconjugated estradiol) between 15 – 18 weeks of gestation. In this, 1 in 195 had risk for Down syndrome. Majority of the chromosomally normal singleton gestations without anomalies who had elevated βhCG developed PIH at term (68%) and had adverse pregnancy outcome.

Feng Q and Cui S conducted a study and reported that serum βhCG maternal levels could reflect the degree of functional imbalance of trophoblast and it may be used as clinical detecting index of PIH.
On the other hand HPL (Human Placental Lactogen) is not such a useful factor.

Roiz –Hern and Cabello-Mart reported that measuring levels of βhCG during second trimester of pregnancy is useful in clinical practice to identify pregnant women who will develop preeclampsia.

Gonen et al and Sharg et al conducted a cohort analytical study to determine whether women with unexplained elevations of maternal serum βhCG at 16 – 20 weeks gestation are at an increased risk for pregnancy complications and adverse pregnancy outcome. The inclusion criteria were singleton gestation, confirmed gestational age and βhCG levels more than 2.5 MOM. The exclusion criteria were foetal anomalies and maternal serum alphafeto protein (AFP) more than 2.5 MOM.
A group of randomly selected women with normal βhCG and maternal serum AFP levels served as control. The results – of 6011 women screened 284 (4.7%) had an unexplained elevated HCG levels. Patients with elevated levels of βhCG had significantly higher risk for preeclampsia (Odds ratio 4.4, C.I. 1.9-10) and foetal growth restriction (Odds ratio 2.8, 95% CI 1-7).

Chandra S and Scott H studied 14,374 women during the period of 1994 – 2000 and concluded that unexplained elevated levels of MSAFP / HCG were associated with increased risk of most pregnancy complications. Increased antenatal surveillance of these patients is important.

Ashour and Lieberman conducted a study to investigate the association of elevated second trimester serum βhCG concentration with subsequent development of preeclampsia. They examined 6286 non diabetic women with singleton pregnancies between 15 – 22 weeks of gestation (from Nov 1, 1991 - Nov 30, 1994). Women with pre-existing hypertension were excluded from the study. Beta HCG levels expressed as

multiples of Median (MOM) adjusted for gestational age was compared between normotensive and hypertension complicating pregnant women. They found increased incidence of preeclampsia in patients with raised serum βhCG levels.

PREECLAMPSIA

Preeclampsia is a disorder of unknown aetiology. It is a clinical syndrome rather than a single disease. Therefore the pathophysiologic abnormalities of this syndrome are heterogenous and vary among predisposed women.

According to the working group of NHBPEP, 2000, hypertensive disorders complicating pregnancy are classified as follows:

1. Gestational hypertension (formerly PIH that included transient hypertension)
2. Preeclampsia
3. Eclampsia
4. Preeclampsia superimposed on chronic hypertension
5. Chronic hypertension

DEFINITION

Gestational hypertension:

- Blood pressure(BP) ≥ 140/90 mm Hg for first time during pregnancy
- No Proteinuria
- BP returns to normal within 12 weeks post partum
- Final diagnosis made only postpartum
- May have other signs and symptoms of preeclampsia

Preeclampsia:

Minimum criteria:

- BP ≥ 140/90 mm Hg after 20 weeks of gestation
- Proteinuria ≥ 300 mg/24 h or ≥ 1+ dipstick

Increased certainity of preeclampsia:

- BP ≥ 160/110 mm Hg
- Proteinuria 2g/ 24 h or ≥ 2+ dipstick
- Serum creatinine > 1.2 mg/dl unless known to be previously elevated.
- Platelets < 1 lakh / cubic mm.
- Microangiopathic haemolysis (increased LDH).
- Elevated ALT/ AST
- Persistent headache or other cerebral or visual disturbance

- Persistent epigastric pain

Eclampsia:

Seizures that cannot be attributed to other causes in a women with preeclampsia.

Superimposed preeclampsia on chronic hypertension

- New onset Proteinuria ≥ 300 mg/24 h in hypertensive women but no Proteinuria before 20 weeks gestation.
- Sudden increase in proteinuria or blood pressure or platelet count < 1 Lakh / cubic mm in a woman with hypertension and proteinuria before 20 weeks gestation.

Chronic hypertension

- BP ≥ 140/90 mm Hg before pregnancy or diagnosed before 20 weeks gestation not attributable to gestational trophoblastic disease.
- Hypertension first diagnosed after 20 weeks of gestation and persistent after 12 weeks postpartum.

ACOG CLASSIFICATION OF HYPERTENSION DURING PREGNANCY

1. Pregnancy induced hypertension

    1.1 transient hypertension

    1.2 preeclampsia

a) mild

b) severe

1.3 eclampsia

2. Pregnancy aggravated hypertension

2.1 superimposed preeclampsia

2.2 superimposed Eclampsia

3. coincidental hypertension

INCIDENCE OF PREECLAMPSIA

Incidence of preeclampsia is 5 – 8 %. In India the incidence is 7-9%.

RISK FACTORS FOR PREECLAMPSIA

1. extremes of age
2. nulliparity
3. obstetric

- preeclampsia in previous pregnancy

- multiple gestation
- hydrops foetalis
- hydatidiform mole

4. pre-existing medical disorders
    - hypertension
    - diabetes mellitus
    - autoimmune disease
    - thrombophilias
5. genetic
    - family history of preeclampsia
6. environmental

FACTORS ASSOCIATED WITH REDUCED RISK OF HYPERTENSION

- Smoking
- Placenta previa

HYPERTENSION

Hypertension during pregnancy is diagnosed when the resting BP is 140/ 90 mm Hg or greater. Korotkoff's phase V is used to define diastolic pressure (**Brown M A and Buddle M C, 1998**). These BP recordings must be recorded on at least two occasions 6 hours or more apart.

EDEMA

Edema is abandoned as a diagnostic criterion, because it occurs in too many normal pregnant women.

PROTEINURIA

Proteinuria is an important sign of preeclampsia. **Chesley**, 1985 concluded that the diagnosis of preeclampsia is questionable in the absence of proteinuria. Significant proteinuria is defined by 24 hrs urinary protein exceeding 300 mg/ 24 hrs or persistent 30 mg/dl (1+ dipstick) in random urine sample. Proteinuria is commonly assessed by dipstick method.

Urinary dipstick	**Protein in urine**
Trace	0.1 g /L
1 +	0.2 g/L
2+	1 g/L
3+	3 g/L
4+	10 g/L

INDICATORS OF SEVERITY OF HYPERTENSIVE DISORDERS OF PREGNANCY

ABNORMALITY	MILD	SEVERE
Diastolic BP	< 100 mm Hg	≥ 110 mm Hg
Proteinuria	Trace – 1+	Persistent 2+/more
Headache	absent	Present
Visual disturbance	absent	Present
Upper abdominal pain	absent	Present
oliguria	absent	Present
convulsions	absent	Present
Serum creatinine	normal	elevated
Thrombocytopenia	absent	Present
Liver enzyme elevation	absent	Present
Foetal growth restriction	absent	Present
Pulmonary oedema	absent	present

OTHER SYSTEMIC EFFECTS OF PREECLAMPSIA

BRAIN : Oedema, haemorrhage, infarction

EYE : Serous retinal detachment, cortical blindness, pappilloedema

CVS : Hypertension, pulmonary oedema

RS : Pulmonary oedema, aspiration pneumonia

LIVER : Congestion, haemorrhage, infarction, rupture

KIDNEY: Glomerulo endotheliosis, nephritic syndrome, acute renal failure

BLOOD: Thrombocytopenia, Microangiopathic haemolytic anaemia, disseminated intravascular coagulation.

REPRODUCTIVE: IUGR, prematurity, placental abruption, foetal demise.

SKIN : Oedema, petechiae, ecchymosis

MUCOSA: Laryngeal oedema

AETIOLOGY OF PREECLAMPSIA

According to Sibai (2003) currently plausible potential causes of preeclampsia include the following:

1. Abnormal trophoblastic invasion of uterine vessels

2. Immunological intolerance between maternal and feto-placental tissues

3. Maternal maladaptation to cardiovascular or inflammatory changes of normal pregnancy

4. Dietary deficiencies

5. Genetic influences

1. ABNORMAL TROPHOBLASTIC INVASION

In normal implantation, the uterine spiral arteries undergo extensive remodelling as they are invaded by endovascular trophoblasts. In preeclampsia, there is incomplete trophoblastic invasion. In this case, there is failure of second wave of trophoblastic invasion. The decidual vessels but not myometrial vessels become lined with endovascular trophoblast. **Madazli** and colleagues (2000) showed that magnitude of defective trophoblastic invasion of spiral arteries correlated with severity of hypertensive disorder.

Obstruction of spiral arteriolar lumen by atherosis may impair placental blood flow which eventually leads to preeclampsia syndrome **(Lain and Roberts, 2002 and Redman, Sargent, 2003).**

2. IMMUNOLOGICAL FACTORS

There is circumstantial evidence to support the theory that preeclampsia is immune mediated. The microscopic changes at the maternal placental interface are

suggestive of acute graft rejection (**Labarrere, 1988**). Risk of preeclampsia is appreciably enhanced in circumstances where formation of blocking antibody to placental antigenic sites might be impaired. This may arise in situations in which effective immunisation by a previous pregnancy is lacking as in first pregnancies or in which the number of antigenic sites provided by the placenta is unusually great compared with amount of antibodies as with multiple foetuses (**Brer,1978**).

Dekker and Sibai (1998) have reviewed the possible role of immune maladaptation in the pathophysiology of preeclampsia. Beginning in early second trimester, women destined to develop preeclampsia have a significantly lower proportion of T Helper cells (TH 1) compared with that of women who remain normotensive (TH1 / TH2 imbalance).

3. VASCULOPATHY AND INFLAMMATORY CHANGES

In response to placental factors released by ischaemic changes or any other inciting cause, cascades of events are set in motion **(Redman and Sargent,** 2003). The decidua also contains an abundance of cells that when activated can release noxious agents (**Staff and colleagues**, 1999). These then serve as mediators to provoke endothelial injury.

Redman and colleagues (1999) have proposed that endothelial cell dysfunction

associated with preeclampsia can result from a generalised perturbation of normal maternal intravascular inflammatory adaptation to pregnancy. In this hypothesis, preeclampsia is considered as a disease due to an extreme state of activated leukocytes in maternal circulation. Oxidative stress is characterised by reactive oxygen species and free radicals that lead to formation of self propagating lipid peroxides (**Manten and associates**, 2005). These in turn generate highly toxic radicals that injure endothelial cells modifying their nitric oxide production and interfere with prostaglandin balance.

4. DIETARY DEFICIENCIES

Mac Gillivray reviewed the available evidence for role of dietary deficiency in the pathogenesis of preeclampsia. It was concluded that such available evidence was unsatisfactory. WHO expert committee on pregnancy and lactation concluded that there was no scientific basis for believing that either deficiencies or excess of any essential nutrient predisposes to preeclampsia. However the possibility does remain that in certain populations there may be specific dietary deficiency that may predispose to or exacerbate the onset of preeclampsia.

When concentration of Calcium is low in extracellular fluid (ECF), the amount of ionic calcium entering the cell will increase, making vascular smooth muscle cells more sensitive to excitation **(Ganong**,1979).

Like calcium, decreased Magnesium levels are thought to potentiate contractile response of vascular smooth muscle to vasopressors **(Prasad et al** , 1980).

The role of dietary deficiencies e.g. Calcium, Magnesium, Free fatty acids in aetiology of hypertensive disorders of pregnancy still remains speculative.

5. GENETIC FACTORS

The predisposition to hereditary hypertension undoubtedly is linked to preeclampsia (**Nese and colleagues**, 2003) and tendency of preeclampsia and eclampsia is highly heritable. **Kilpatrick and associates** (1989) reported an association between histocompatibility antigen (HLA- DR4) and proteinuric hypertension.

PATHOGENESIS OF PREECLAMPSIA

VASOSPASM

The concept of vasospasm was advanced by **Volhard** (1918) based on direct observation of small blood vessels in nail beds, ocular fundi and bulbar conjunctiva. Endothelial cell damage causes interstitial leakage through which blood constituents including platelets and fibrinogen are deposited subendothelially.

ENDOTHELIAL CELL ACTIVATION

Over the past two decades endothelial cell activation has become the centre piece

in contemporary understanding of pathogenesis of preeclampsia. In this scheme, unknown factors likely from placenta are secreted in to the maternal circulation and provoke activation & dysfunction of vascular endothelium. The clinical syndrome of preeclampsia is thought to result from these widespread endothelial cell changes.

INCREASED PRESSOR RESPONSES

Women with early preeclampsia have increased vascular reactivity to infused norepinephrine and Angiotensin II.

Prostaglandins **:** When compared to normal pregnancy, endothelial prostacyclin (PG I2) production is decreased in preeclampsia. At the same time, Thrombaxane A2 (TXA2) secretion by platelets is increased and PG I2 / TXA2 ratio decreases.

Nitric oxide **:** Nitric oxide (NO) previously termed endothelial derived relaxing factor (EDRF) is synthesised by endothelial cells from L-Arginine (Palmer and associates, 1988). It is a potent dilator whose absence or decreased concentration might play a role in the aetiology of PIH.

Endothelins: These 21 aminoacid peptides are potent vasoconstrictors and endothelin-1 (ET1) is primary isoform produced by human endothelium (Mastrogiannis and co-workers, 1997).

Plasma endothelin-1 is increased in normotensive pregnant women but women

with preeclampsia have even higher levels.

ANGIOGENIC FACTORS

Several glycosylated glycoproteins are selectively angiogenic and are thought to be important in mediating preeclampsia syndrome. Two of these are VEGF (Vascular endothelial growth factor) and PLGF (platelet growth factor).

HUMAN CHORIONIC GONADOTROPHIN (hCG)

Human chorionic gonadotrophin is a glycoprotein, a peptide framework to which carbohydrate side chains are attached. Half life of hCG is 24 hours. HCG consist of 2 subunits, non-covalently linked by disulphide bonds, called alpha and beta. The α subunit is identical to FSH, LH, TSH and consist of 92 aminoacids. Unique biological activity as well as specificity in immunoassays is attributed to the molecular and carbohydrate differences in β subunit. The β subunit contains a larger carbohydrate moiety and 145 amino acid residues including a unique carboxy terminal tail piece of 23 amino acid groups. It is this unique part of HCG structure that allows production of highly specific antibodies and utilization of highly specific immunological assays.

HCG is mainly synthesized by syncytiotrophoblasts. The maternal circulating HCG

concentration is approximately 100 IU/L at the time of expected but missed menses. The maximum level of about 1,00,000 IU /L in maternal circulation is reached at 8 – 10 weeks gestation. HCG levels decrease to about 10,000 – 20,000 IU / L by 18-20 weeks of gestation and remain at that level until delivery.

All human tissues appear to make HCG in small amounts but the placenta is different in having the ability to glycosylate the protein, thus reducing the rate of metabolism and giving it biological activity through long half life. HCG produced in sites other than placenta has little or no carbohydrate moiety and therefore it has a very short half life and rapidly clears from the circulation through the kidneys.

HCG becomes detectable in maternal serum as early as 8 -10 days after ovulation in normal conception cycles. In a normally progressing early intrauterine pregnancy, βhCG levels should increase at least 66% every 48 hours at concentration below 10,000 IU/L.

Biosynthesis of HCG: (Genetics of HCG)

The alpha subunit originates from one single gene in chromosome 6, the beta subunits are from chromosome 19. There are 8 separate genes for beta subunits of different glycoprotein hormones.

REGULATION OF HCG SYNTHESIS

HCG secretion is probably regulated by the following factors, although the exact mechanism has not yet been identified.

1. Placental GnRH (Gonadotrophin releasing hormone) and CRH (Corticotrophin releasing hormone)
2. Butyrated cyclic AMP
3. Interleukin – 1 and interleukin – 6
4. Tumour necrosis factor (TNF)
5. Trophoblastic Growth Factor (TGF –B)
6. Fibroblast Growth Factor

FUNCTIONS OF HCG

1. Both subunits of HCG have a binding tendency to the LH / HCG receptor. It is this binding that is most marked in the tissues of corpus luteum
2. Rescue of corpus luteum - Soon after embedding of the ovum, the fertilized ovum needs a support for survival for which continued Progesterone is necessary. The Progesterone at this stage of pregnancy is available only from corpus luteum. Hence the life of the corpus luteum needs to be prolonged beyond 2 weeks after the

expected date of menstruation and this prolongation of the life of corpus luteum is provided by the HCG and probably is the only explanation of HCG function in the early pregnancy

3. HCG promotes relaxin secretion by the corpus luteum. Further HCG is also believed to promote vascular dilatation and myometrial relaxation providing support to the fertilized ovum.

NORMAL SERUM βhCG VALUES IN PREGNANCY

GESTATIONAL AGE weeks	**MEDIAN IU/ ml.**	**RANGE IU /ml.**
4	1.1	0.04 – 4.48
5	8.05	0.27 – 28.7
6	29.7	3.7 – 84.9
7	58.8	9.7 – 120
8	79.5	31.0 – 184
9	91.51	61.5 – 182
10	71.01	22.0 – 143
14	34.91	15.0 - 92
15	26.81	10.6 – 64.2
16	21.2	9 – 52.8
17	19.1	6.7 – 47.1
18	15.6	6.1 – 42.1
19	15.2	6.8 – 45.9
20	15.1	6.3 – 44

ELISA (ENZYME LINKED IMMUNOSORBANT ASSAY)

It is useful for quantification of extremely small amounts of βhCG. ELISA test uses monoclonal antibodies bound to a solid phase support which binds the βhCG in the sample. A second antibody is added to sandwich the test sample βhCG. The second antibody is linked with an enzyme such as Alkaline Phosphatase. When the substrate for this enzyme is added, blue colour develops. The intensity of which is proportional to the amount of enzyme and thus to the amount of second antibody bound. This in turn is a function of the amount of βhCG in the test sample. The sensitivity of the test is 25 – 50 mU/ml.

AIM OF STUDY

1. To estimate Serum β hCG levels in early 2nd trimester in a population of high risk Multigravid women

2. To study any positive correlation between elevated serum βhCG and the development of preeclampsia.

MATERIALS AND METHODS

Study design: Prospective case control study

Study place: Institute of Obstetrics and Gynaecology, Egmore, Chennai.

Study period: April, 2007 – April, 2008.

This study was conducted in 200 cases of high risk multi gravid women attending outpatient department of Institute of Obstetrics and Gynaecology, Chennai.

This study was approved by the board of ethical committee.

METHODOLOGY

200 cases of high risk multigravid women attending outpatient department of IOG with normal blood pressure and normal urine examination of gestational age 15 – 20 weeks were taken for the study after obtaining informed consent. The high risk factors included in the study were previous history of preeclampsia remote from term(< 34 weeks), recurrent spontaneous abortions (2 or more), previous still births, accidental haemorrhage, IUGR, eclampsia. Detailed history and physical examination including blood pressure, urine examination, and abdominal examination were done. Other baseline investigations like Hb, PCV, blood sugar, USG were done to rule out anaemia, diabetes, multiple pregnancies, anomalous babies and wrong dates. About 5 ml of

venous blood was taken at 15 to 20 weeks gestation and serum βhCG estimated by ELISA method using Chemiluscence technique. Patients were divided into two groups based on their serum βhCG values – 1) those with elevated serum βhCG (≥2 MOM) 2) those with normal serum βhCG values (<2 MOM). Both groups of patients were followed up fortnightly up to 28 weeks and then weekly till delivery. During each visit general examination including blood pressure recording, urine examination for sugar and protein, abdominal examination to assess foetal growth & wellbeing and liquor status were done.

To ensure accurate reading of blood pressure and appropriate size BP cuff was used (12 x 23 cm for normal size arm and for arm size more than 35 cm cuff size 15 x 33 cm). BP was recorded after a rest period of 10 min., with the patient in sitting posture with the arm at the level of heart.

The results were analysed using Chi-square and two sample t test using SPSS version 11.5 software.

INCLUSION CRITERIA

Multigravid women with previous history of

i. PIH remote from term (less than 34 weeks)

ii. Recurrent spontaneous abortion (two or more)

iii. Still birth

iv. Accidental haemorrhage

v. IUGR

vi. Eclampsia.

EXCLUSION CRITERIA

a. Gestational age < 15 weeks or >20 weeks

b. Women with Chronic hypertension

c. Other medical disorders complicating pregnancy such as Diabetes, Anaemia, Thyroid, SLE.

d. Multiple pregnancies

e. Babies with suspected or confirmed congenital anomalies detected by USG

RESULTS

TABLE-1 : AGE GROUP

Age group	No. Of cases	Percent
< 20 years	6	3
21 - 25	99	49.5
26 – 30	95	47.5
TOTAL	200	100

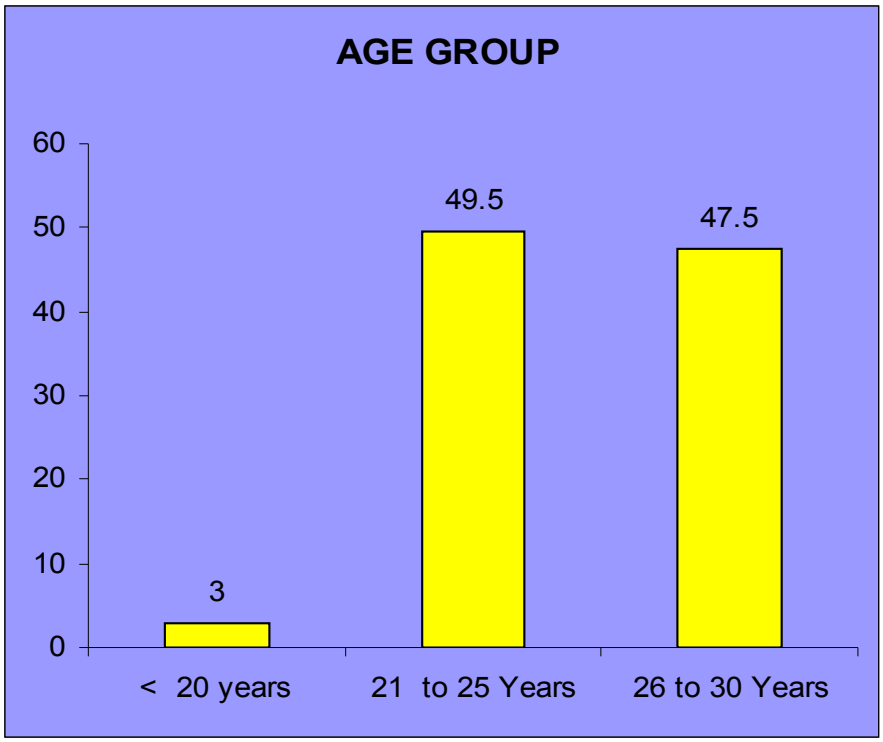
Majority of cases were in the age group of 21 – 25 years (49.5%). Only 6 cases were in the age group of < 20 years.

AGE DISTRIBUTION IN RELATION TO DEVELOPMENT OF PREECLAMPSIA

AGE GROUP	NO. OF CASES THAT DEVELOPED PREECLAMPSIA	PERCENTAGE
< 20 YEARS	6	6.38%
21 – 25 YEARS	41	43.62%
26 – 30 YEARS	47	50%

Majority of cases that developed preeclampsia belonged to the age group of 26 – 30 years (50%). All 6 cases in the age group of ≤ 20 years developed preeclampsia.

AGE DISTRIBUTION



AGE DISTRIBUTION IN RELATION TO DEVELOPMENT OF PREECLAMPSIA

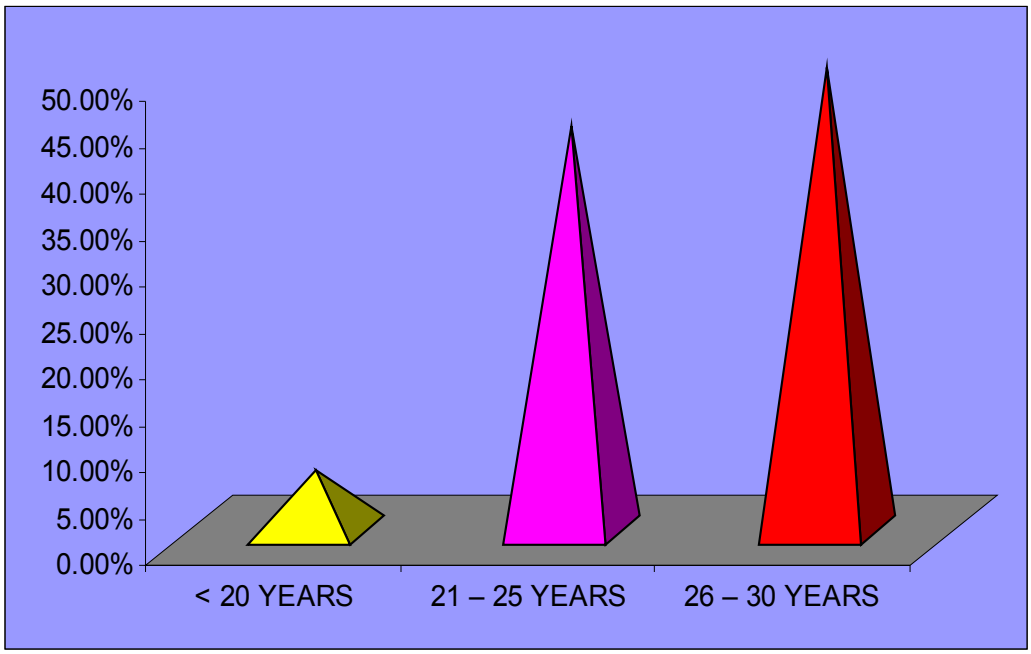


TABLE-2 : SOCIOECONOMIC STATUS

SOCIO ECONOMIC CLASS	NO.OF CASES	PERCENTAGE
III	4	2
IV	31	15.5
V	165	82.5

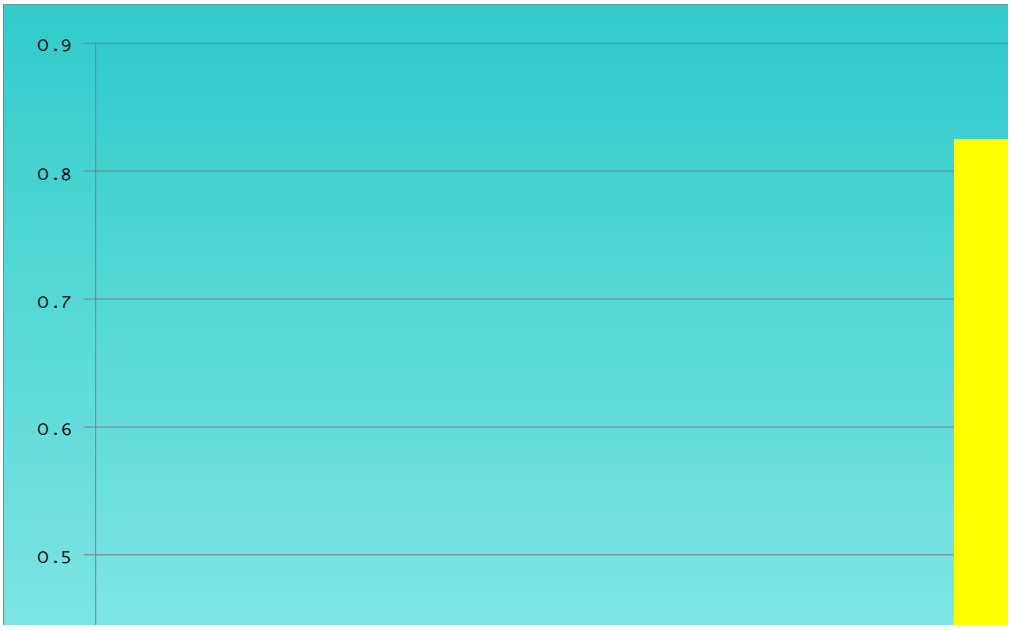
Most of the cases (82.5%) belonged to socioeconomic class V. This is an expected one as our hospital serves very low socioeconomic class patients.

SOCIOECONOMIC CLASS IN RELATION TO DEVELOPMENT OF PREECLAMPSIA

SOCIOECONOMIC CLASS	NO. OF CASES THAT DEVELOPED PREECLAMPSIA	PERCENTAGE
III	4	4.25
IV	23	24.46
V	67	71.27

Most of the cases that developed preeclampsia also belonged to socioeconomic class V (71.27%).

SOCIOECONOMIC STATUS



SOCIOECONOMIC CLASS IN RELATION TO DEVELOPMENT OF PREECLAMPSIA

TABLE -3 : PARITY

GRAVIDA	NO. OF CASES	PERCENTAGE
2	113	56.5
3	63	33
4	18	9
5	3	1.5

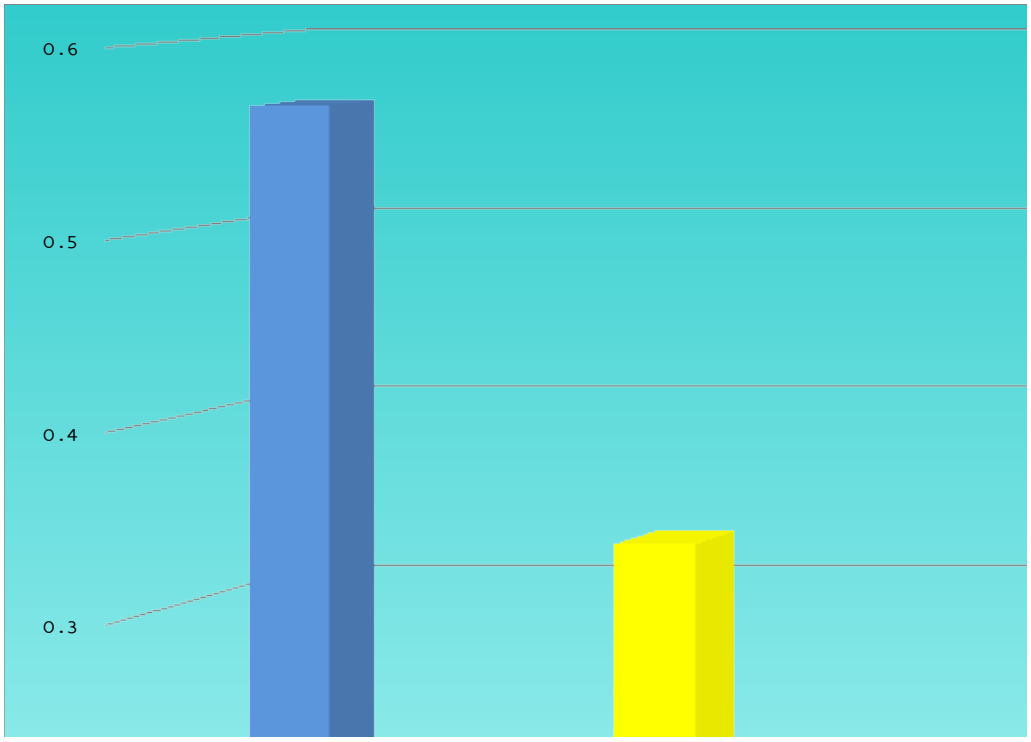
About 56.5% of cases were second gravidae; only 1.5% of cases were gravida 5.

PARITY IN RELATION TO PREECLAMPSIA

GRAVIDA	NO. OF CASES THAT DEVELOPED PREECLAMPSIA	PERCENTAGE
GRAVIDA 2	58	61.70%
GRAVIDA 3	28	29.79%
GRAVIDA 4	7	7.45%
GRAVIDA 5	1	1.06%

About 61.70% of cases that developed preeclampsia were of gravida 2.

PARITY DISTRIBUTION



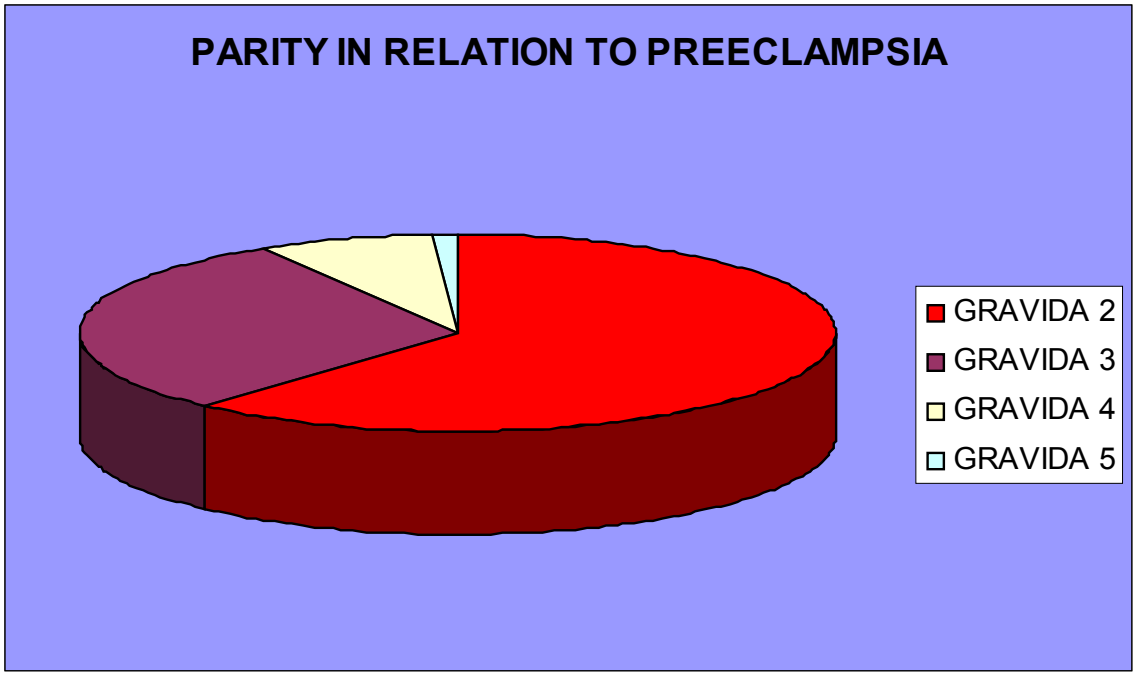


TABLE - 4 : DISTRIBUTION OF GESTATIONAL AGE AT WHICH BLOOD SAMPLE FOR SERUM βhCG WAS TAKEN

GESTATIONAL AGE IN WEEKS	NO.OF CASES	PERCENTAGE
15	7	3.5%
16	94	47%
17	56	28%
18	32	16%
19	6	3%
20	5	2.5%

Majority of the blood samples were taken at the gestational age of 16 weeks (47%).

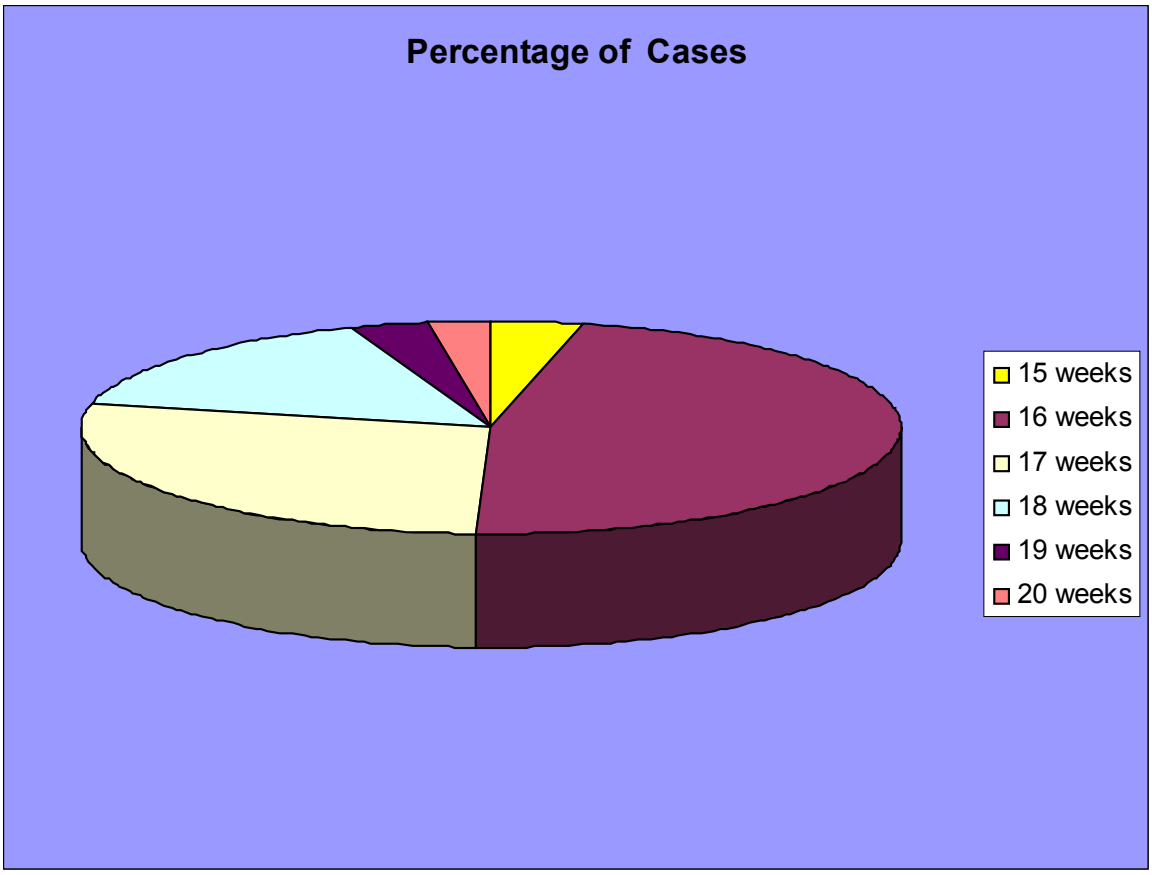

Percentage of Cases
15 weeks
16 weeks
17 weeks
18 weeks
19 weeks
20 weeks

TABLE - 5 : COMPARISON OF GESTATIONAL AGE AT WHICH SERUM βhCG WAS TAKEN BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

SERUM βhCG	NO. OF CASES	MEAN GESTATIONAL AGE
≥2 MOM	106	16.7075
<2 MOM	94	16.8085

P = 0.490 (NOT SIGNIFICANT).

There was no statistically significant difference in gestational age at which serum βhCG was taken between the normal and elevated βhCG groups.

COMPARISON OF GESTATIONAL AGE AT WHICH SERUM βhCG WAS TAKEN BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

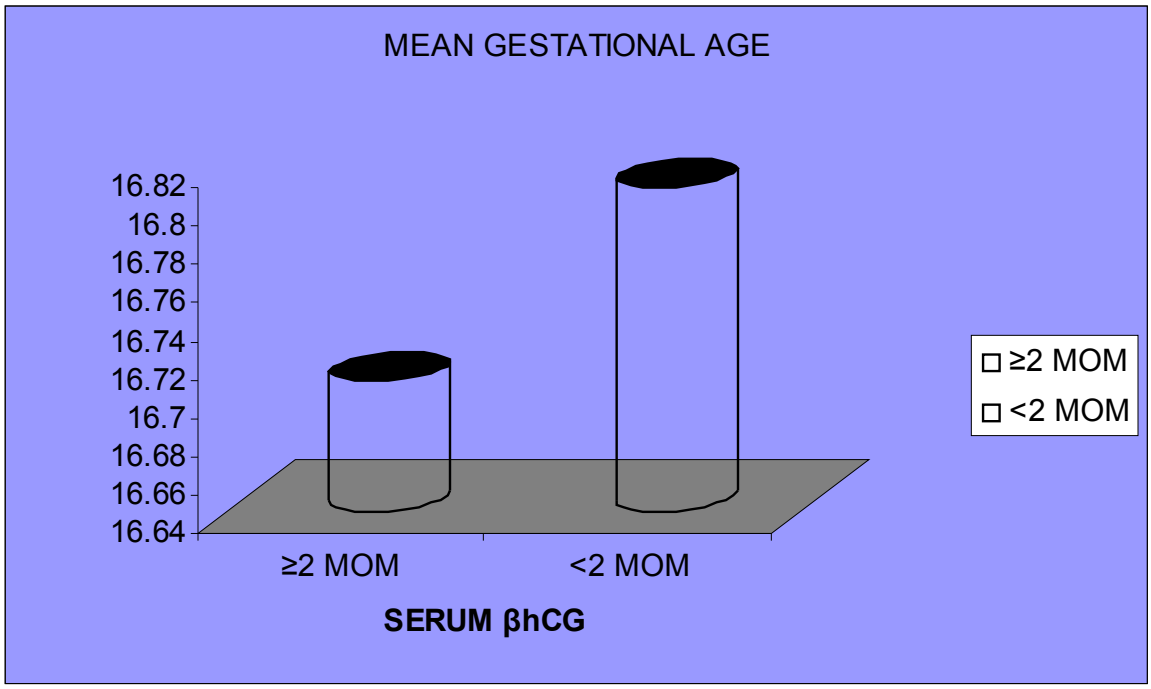


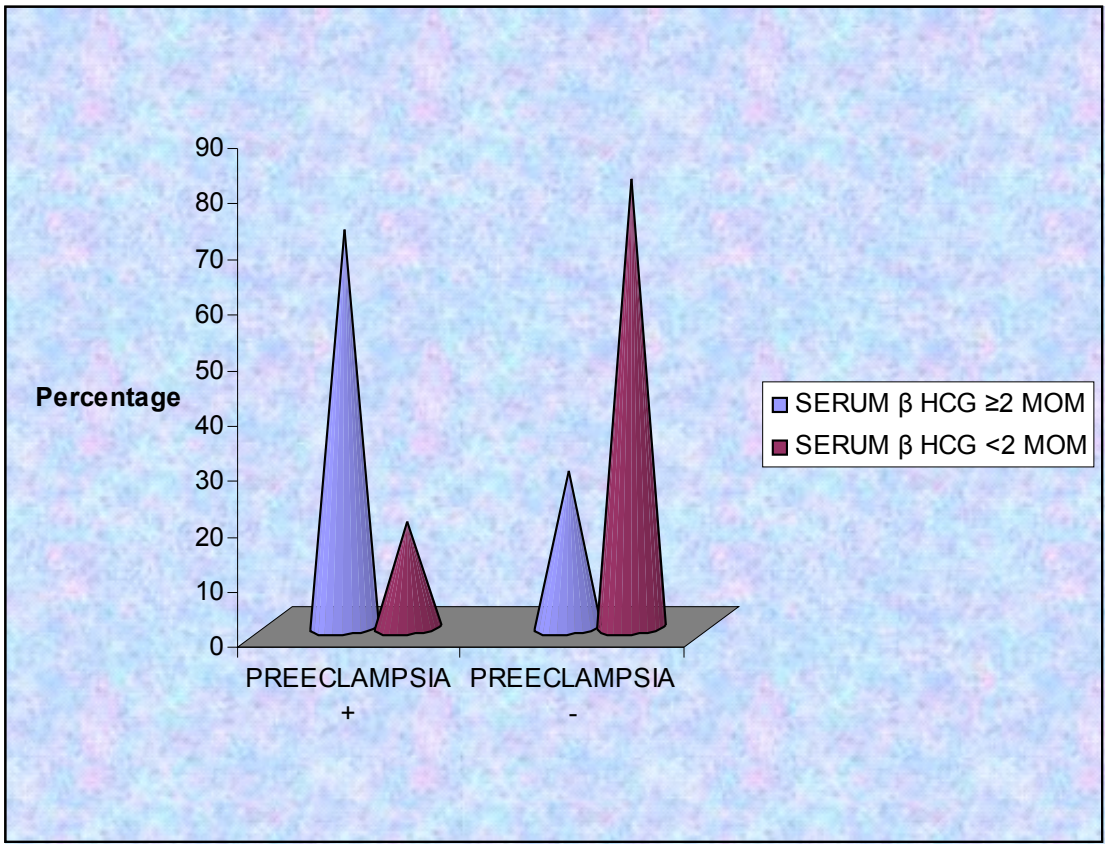
TABLE - 6: COMPARISON OF DEVELOPMENT OF PREECLAMPSIA BETWEEN NORMAL AND ELEVATED HCG GROUPS

	SERUM β HCG		**TOTAL**
	≥2 MOM	**<2 MOM**	
PREECLAMPSIA +	76 (71.7%)	18 (19.1%)	94
PREECLAMPSIA -	30 (28.3)	76(80.9%)	106
TOTAL	106	94	200

P = <0.001(SIGNIFICANT)

Out of 106 cases with elevated serum βhCG values 76 patients developed preeclampsia (71.7%). This is in contrast to 94 cases with normal βhCG values of which only 18 cases (19.1%) developed preeclampsia. This is statistically significant with P value less than 0.001.

COMPARISON OF DEVELOPMENT OF PREECLAMPSIA BETWEEN NORMAL AND ELEVATED HCG GROUPS



EVALUATION OF SERUM βhCG AS A SCREENING TEST IN PREDICTING PREECLAMPSIA:

SERUM βhCG	PREECLAMPSIA		TOTAL
	YES	NO	
≥2 MOM	76 (a)	30 (b)	106
<2 MOM	18 (c)	76 (d)	94

Sensitivity = a / a+c x 100 = 76 / 76+18 x 100 = 80.85%

Specificity = b / b+d x 100 = 30 /30+76 x 100 = 71.7%

Positive predictive value = a / a+b x 100 = 76 / 76+30 x 100 = 71.7%

Negative predictive value = d/ c+d x 100 = 76 /76+18 x 100 = 80.85%

Diagnostic accuracy of the test is 76% (Wilson's score).

Thus evaluation of serum βhCG at 15 – 20 weeks of gestation predicts preeclampsia with a sensitivity of 80.85%, specificity of 71.7%, and positive predictive value of 71.7% and negative predictive value of 80.85%.

TABLE-7: COMPARISON OF GESTATIONAL AGE AT WHICH PREECLAMPSIA DEVELOPED BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

SERUM β HCG	NO. OF CASES THAT DEVELOPED PREECLAMPSIA	MEAN GESTATIONAL AGE AT WHICH PREECLAMPSIA DEVELOPED
≥2 MOM	76	34.9737
<2 MOM	18	36.1667

P = 0.035 (SIGNIFICANT)

The average gestational age at which preeclampsia developed in patients with elevated serum βhCG was 34.97 weeks. This is significantly earlier when compared to the average gestational age of 36.16 weeks at which preeclampsia developed in patients with normal serum βhCG values.

COMPARISON OF GESTATIONAL AGE AT WHICH PREECLAMPSIA DEVELOPED BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

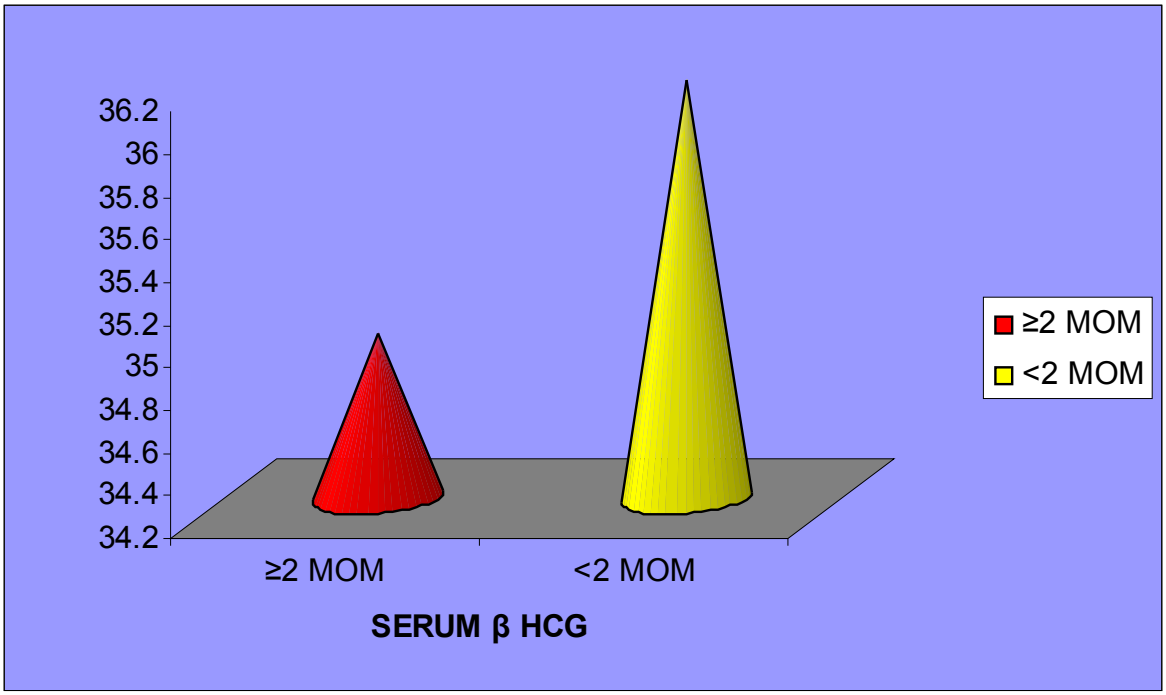

36.2
36
35.8
35.6
35.4
35.2
35
34.8
34.6
34.4
34.2
≥2 MOM
<2 MOM
SERUM β HCG
≥2 MOM
<2 MOM

TABLE-8 : COMPARISON OF DEVELOPMENT OF COMPLICATIONS BETWEEN THE NORMAL AND ELEVATED HCG GROUPS:

COMPLICATIONS	SERUM β HCG		TOTAL
	≥2 MOM	<2 MOM	
NO COMPLICATIONS	97 (91.5%)	92 (97.9%)	189
ABRUPTION	2 (1.9%)	0 (0.0%)	2
ECLAMPSIA	2 (1.9%)	1 (1.1%)	3
HELLP	1 (0.9%)	0 (0.0%)	1
IUGR	3 (2.8%)	1 (1.1%)	4
PUL. EDEMA	1 (0.9%)	0 (0.0%)	1

P=1.000 (NOT SIGNIFICANT)

Of the 11 complications that developed totally only 2(18.18%) were in the normal serum βhCG group. Remaining 9 (81.82%) were in the elevated serum βhCG group.

COMPARISON OF DEVELOPMENT OF COMPLICATIONS BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

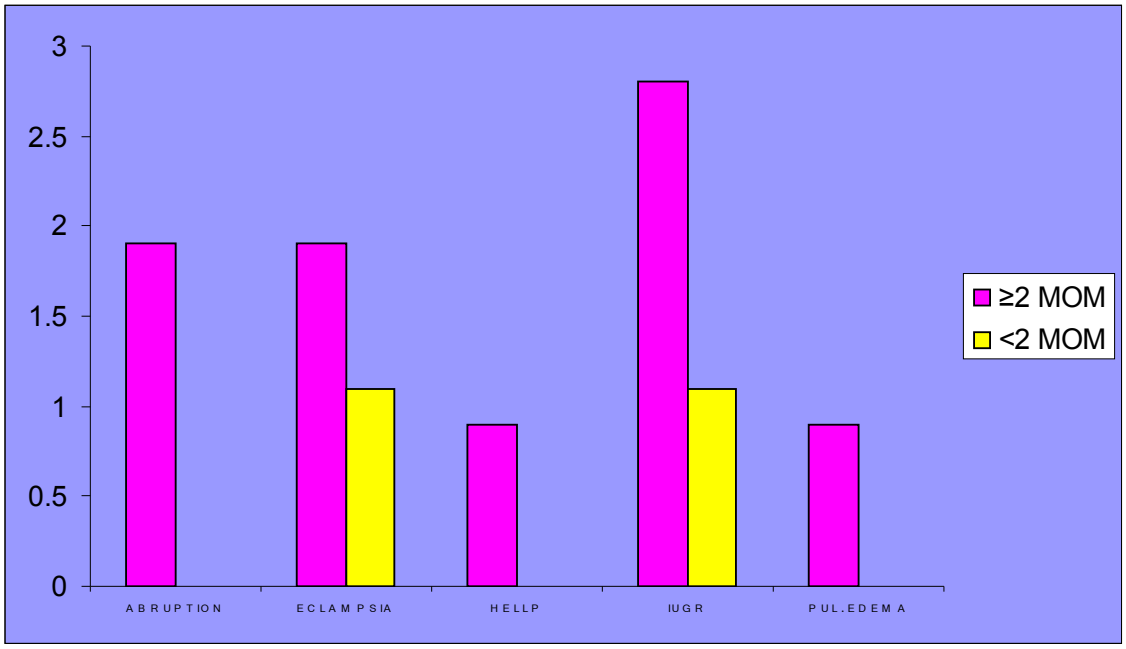


TABLE-9 : COMPARISON OF GESTATIONAL AGE AT DELIVERY BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

GESTATIONAL AGE AT DELIVERY	SERUM βhCG		TOTAL
	≥2 MOM	<2 MOM	
PRETERM (<37 WEEKS)	5 (4.72%)	3 (3.19%)	8
TERM (≥ 37 WEEKS)	101 (95.28%)	91(96.81%)	192
TOTAL	106	94	200

P = 0.752[NOT SIGNIFICANT]

No significant difference was found in the incidence of preterm deliveries between the normal and elevated βhCG groups.

COMPARISON OF GESTATIONAL AGE AT DELIVERY BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

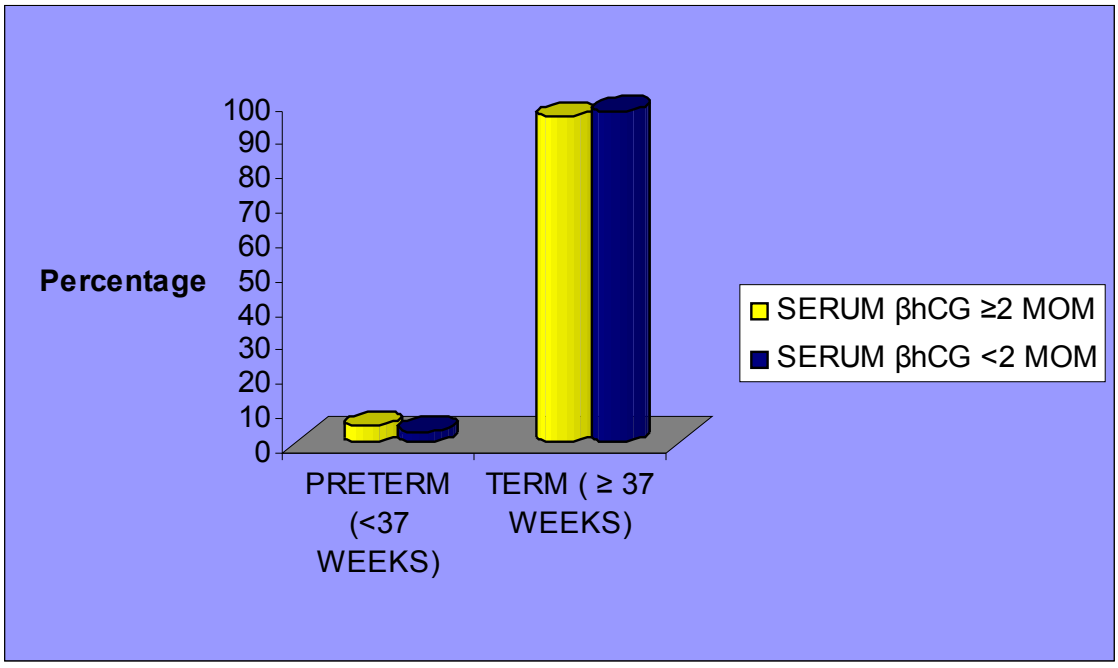


TABLE-10 : COMPARISON OF AVERAGE GESTATIONAL AGE AT DELIVERY BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

SERUM βhCG	NO.OF CASES	MEAN GESTATIONAL AGE AT DELIVERY In WEEKS
≥2 MOM	106	38.5000
<2 MOM	94	39.5426

P = 0.001 (SIGNIFICANT)

The average gestational age at delivery was 38.5 weeks in patients with elevated serum βhCG values and 39.5 weeks in patients with normal serum βhCG values. This is statistically significant.

COMPARISON OF AVERAGE GESTATIONAL AGE AT DELIVERY BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

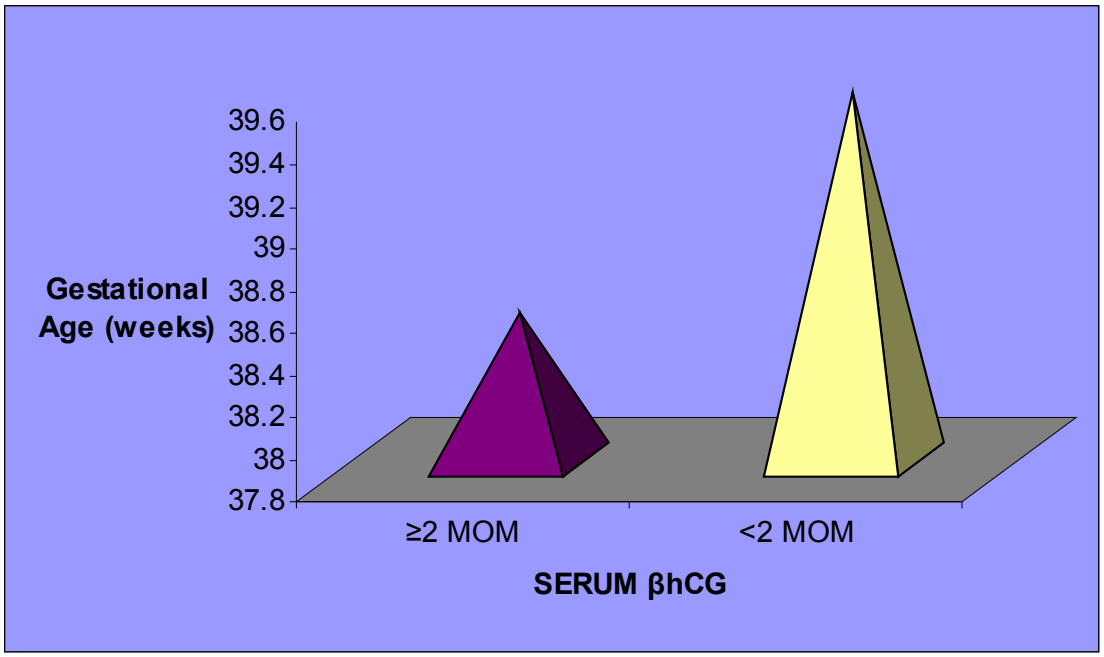


TABLE - 11 : COMPARISON OF MODE OF DELIVERY BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

MODE OF DELIVERY	SERUM βhCG		TOTAL
	≥2 MOM	<2 MOM	
SPONTANEOUS VAGINAL DELIVERY	58 (54.7%)	54 (57.4%)	112
INSTRUMENTAL VAGINAL DELIVERY	3 (2.8%)	1 (1.1%)	4
LSCS	45 (42.5%)	39 (41.5%)	84

TOTAL	106	94	200

P = 0.652 (NOT SIGNIFICANT).

There was no statistically significant difference in the mode of delivery between the normal and elevated serum βhCG groups.

COMPARISON OF MODE OF DELIVERY BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

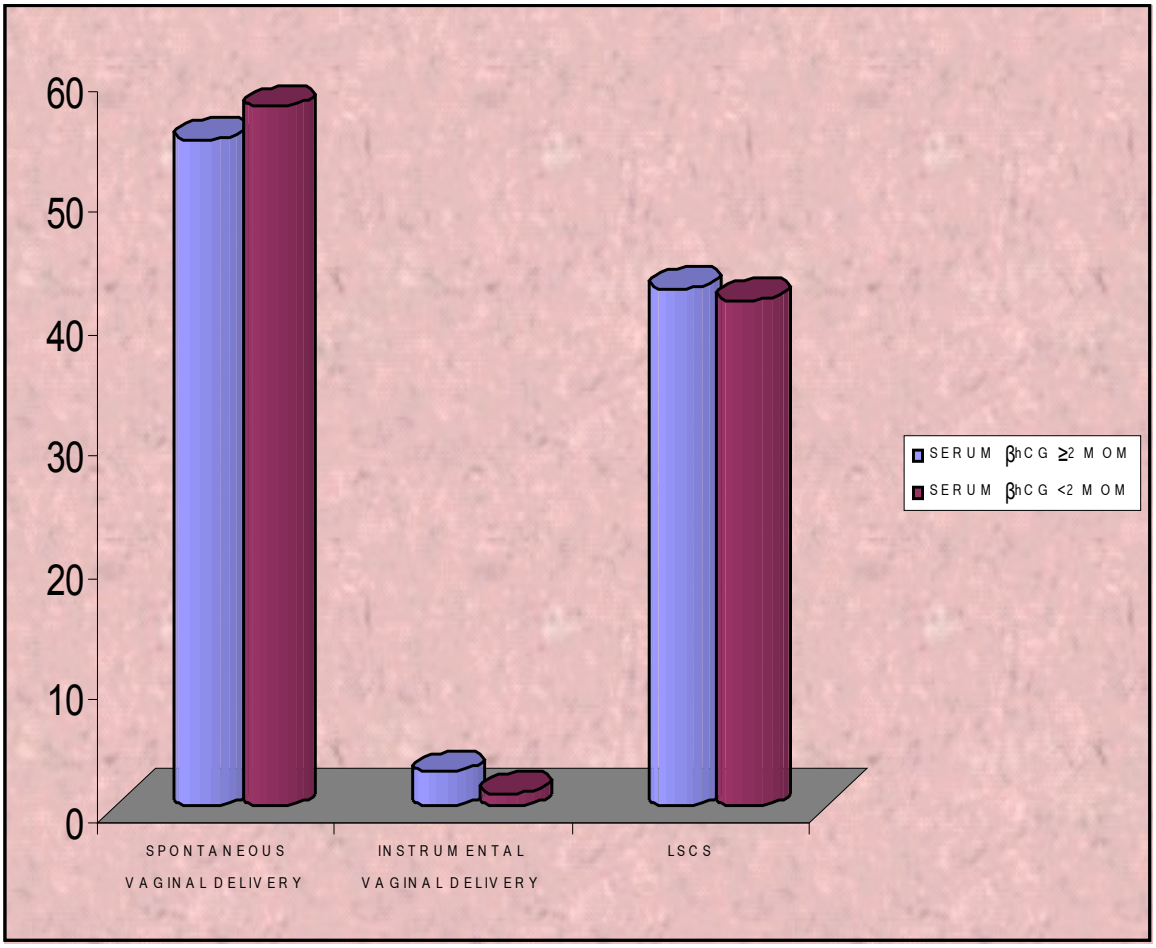

60
50
40
30
20
10
0
SERUM βhCG ≥2 MOM
SERUM βhCG <2 MOM
SPONTANEOUS VAGINAL DELIVERY
INSTRUMENTAL VAGINAL DELIVERY
LSCS

TABLE-12: COMPARISON OF MEAN BIRTH WEIGHT BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

SERUM βhCG	NO. OF CASES	MEAN BIRTH WEIGHT
≥2 MOM	106	2.800
<2 MOM	94	2.9038

P = 0.042 (SIGNIFICANT)

The average birth weight for patients with elevated serum βhCG values was 2.8 weeks when compared to 2.9 weeks in patients with normal serum βhCG values. This is statistically significant.

COMPARISON OF MEAN BIRTH WEIGHT BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

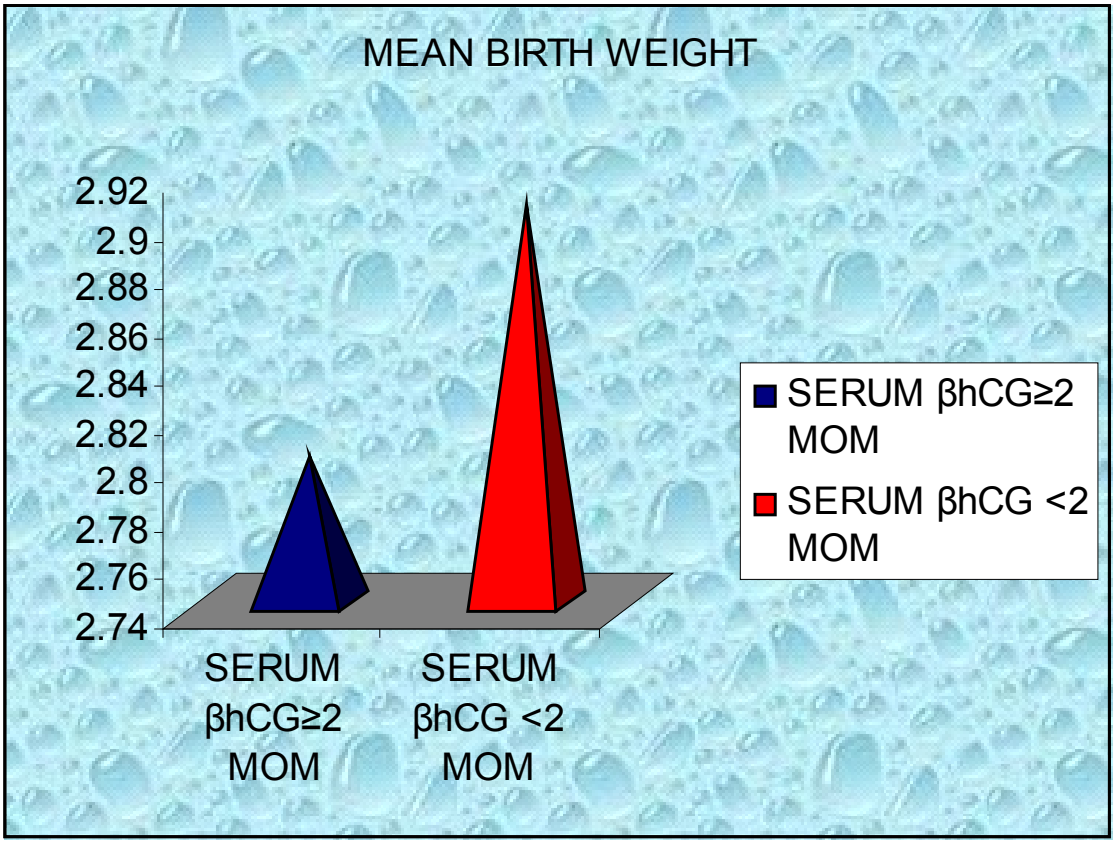


TABLE-13: COMPARISON OF BIRTH WEIGHT BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

BIRTH WEIGHT	SERUM βhCG		TOTAL
	≥2 MOM	<2 MOM	
≥2.5 Kg	82 (77.4%)	78 (83.0%)	160
<2.5 Kg	24 (22.6%)	16 (17.0%)	40
TOTAL	106	94	200

COMPARISON OF BIRTH WEIGHT BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

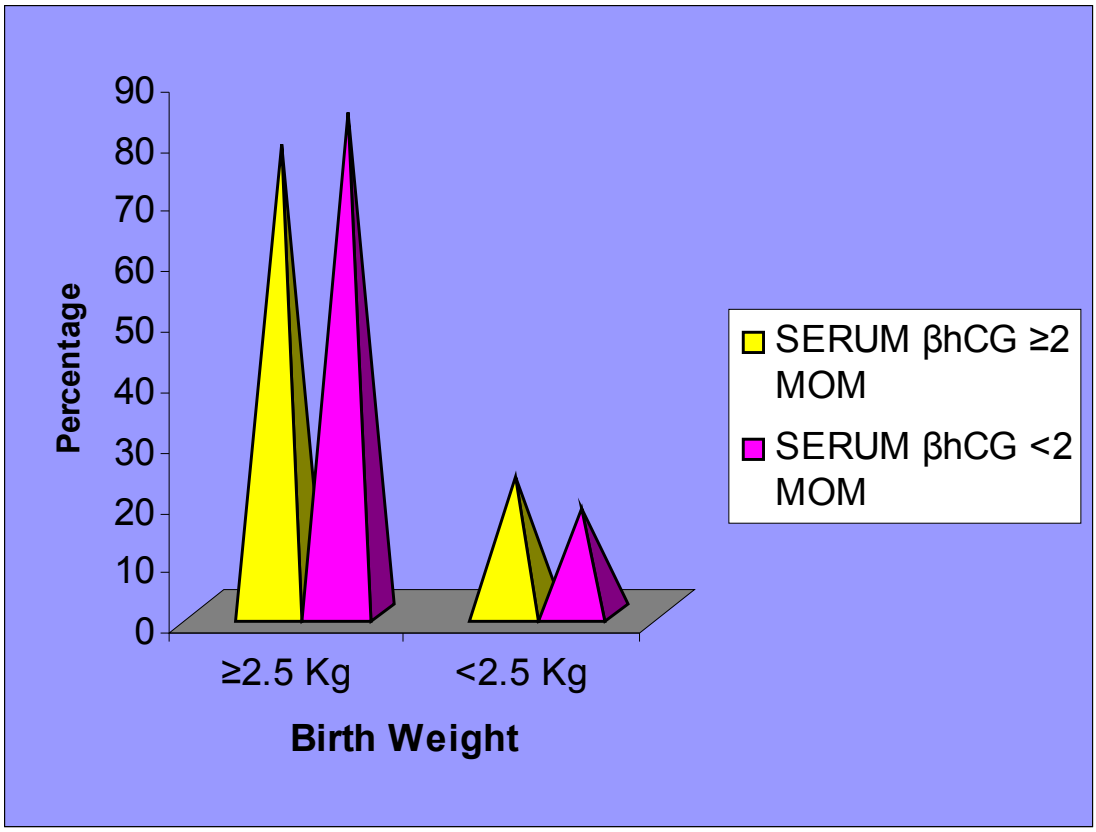


TABLE-14: COMPARISON OF 5-MINUTE APGAR BETWEEN THE NORMAL AND ELEVATED HCG GROUPS:

APGAR	SERUM βhCG		TOTAL
	≥2 MOM	<2 MOM	
0	2 (1.9%)	0 (0.00%)	2
≥7	95 (89.6%)	90 (95.7%)	185
<7	9 (8.5%)	4 (4.3%)	13

P = 0.187 (NOT SIGNIFICANT)

Out of 13 cases with less than score 7 of five minute APGAR, 9 were from elevated serum βhCG group and 4 from normal serum βhCG group. There were 2 still born babies in elevated HCG group and none in normal HCG group.

COMPARISON OF 5-MINUTE APGAR BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

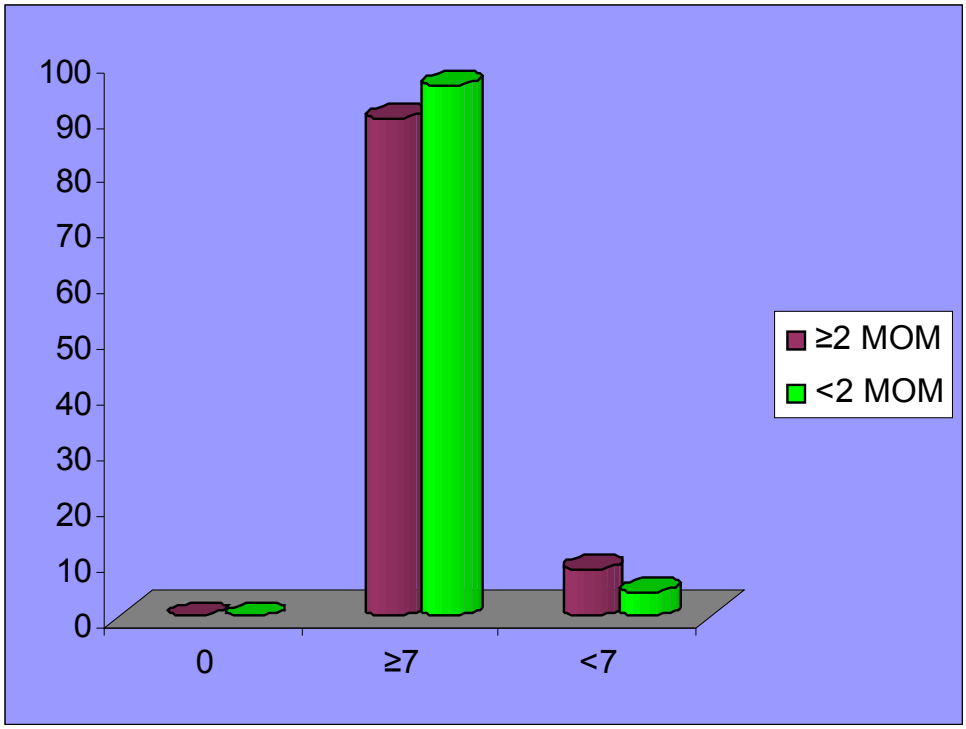


TABLE-15: COMPARISON OF NICU ADMISSION BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

NICU ADMISSION	SERUM βhCG		TOTAL
	≥2 MOM	<2 MOM	
NO	96 (90.6%)	87 (92.6%)	183
YES	10 (9.4%)	7 (7.4%)	17
TOTAL	106	94	200

P = 0.800 (NOT SIGNIFICANT)

Out of 17 babies admitted in NICU, 10 babies (58.82%) were from elevated HCG group and 7(41.17%) from normal HCG group. This is not statistically significant.

COMPARISON OF NICU ADMISSION BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

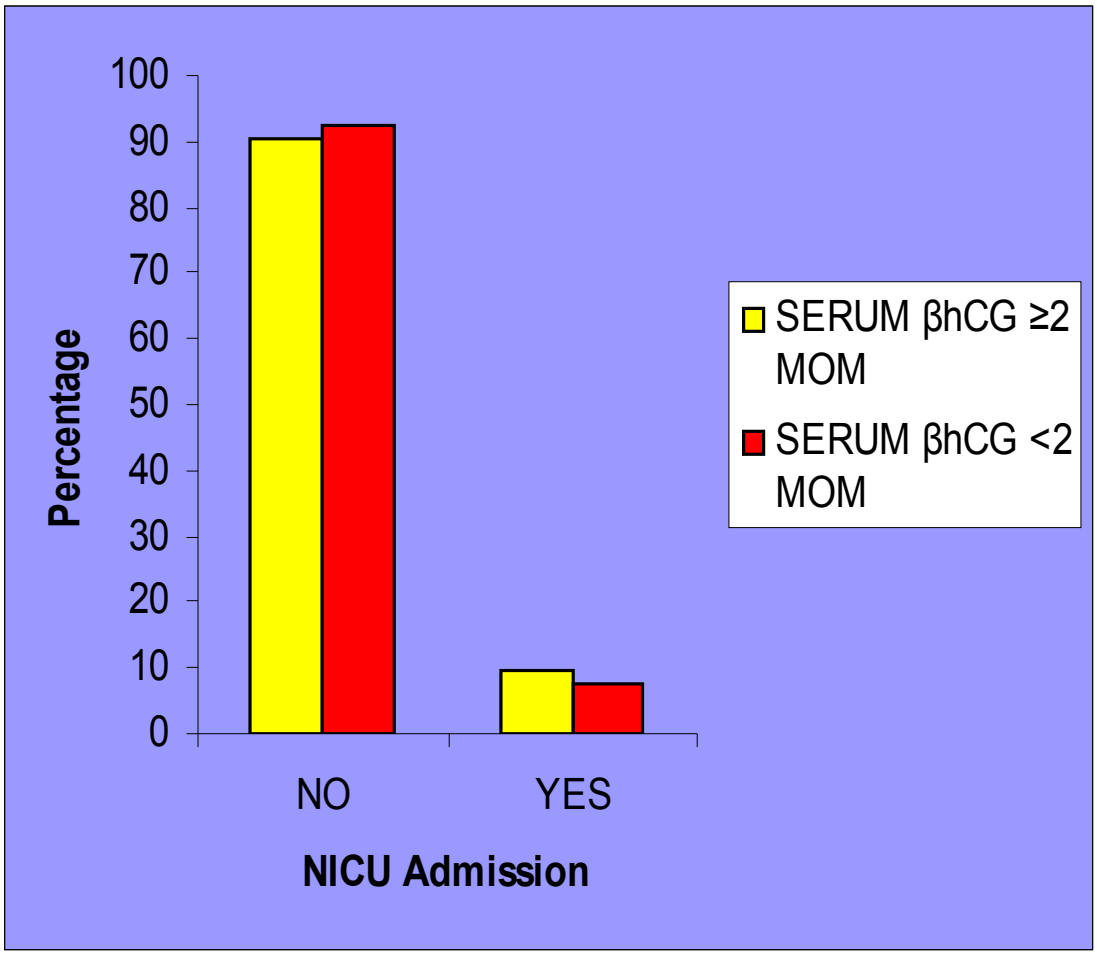


TABLE-16: COMPARISON OF NEONATAL DEATHS BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

NEONATAL OUTCOME	SERUM βhCG		TOTAL
	≥2 MOM	<2 MOM	
NO DEATH	101 (95.3%)	93 (98.9%)	194
NEONATAL DEATH	5 (4.7%)	1 (1.1%)	6
TOTAL	106	94	200

P = 0.217 (NOT SIGNIFICANT).

There were 6 neonatal deaths of which 5 were in the elevated serum βhCG group and only 1 in normal HCG group. This is not statistically significant.

COMPARISON OF NEONATAL DEATHS BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

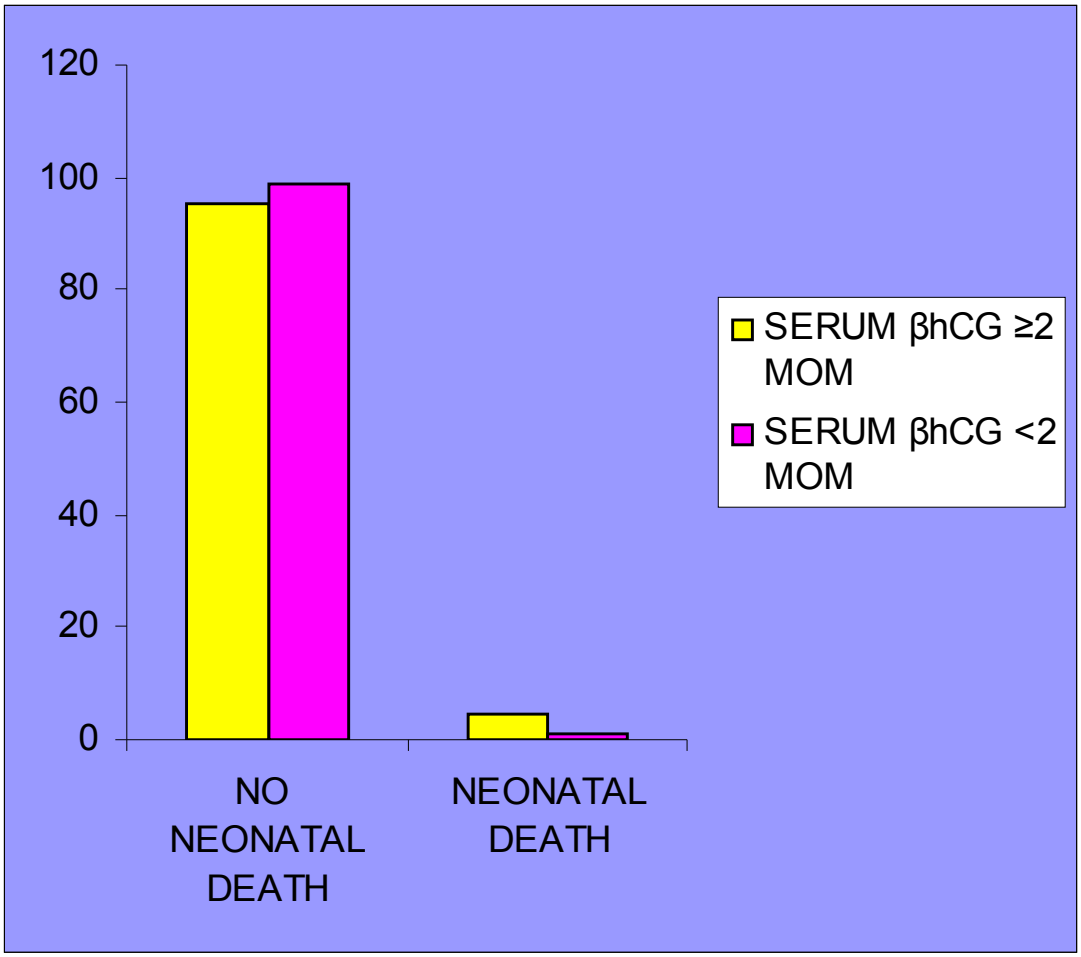


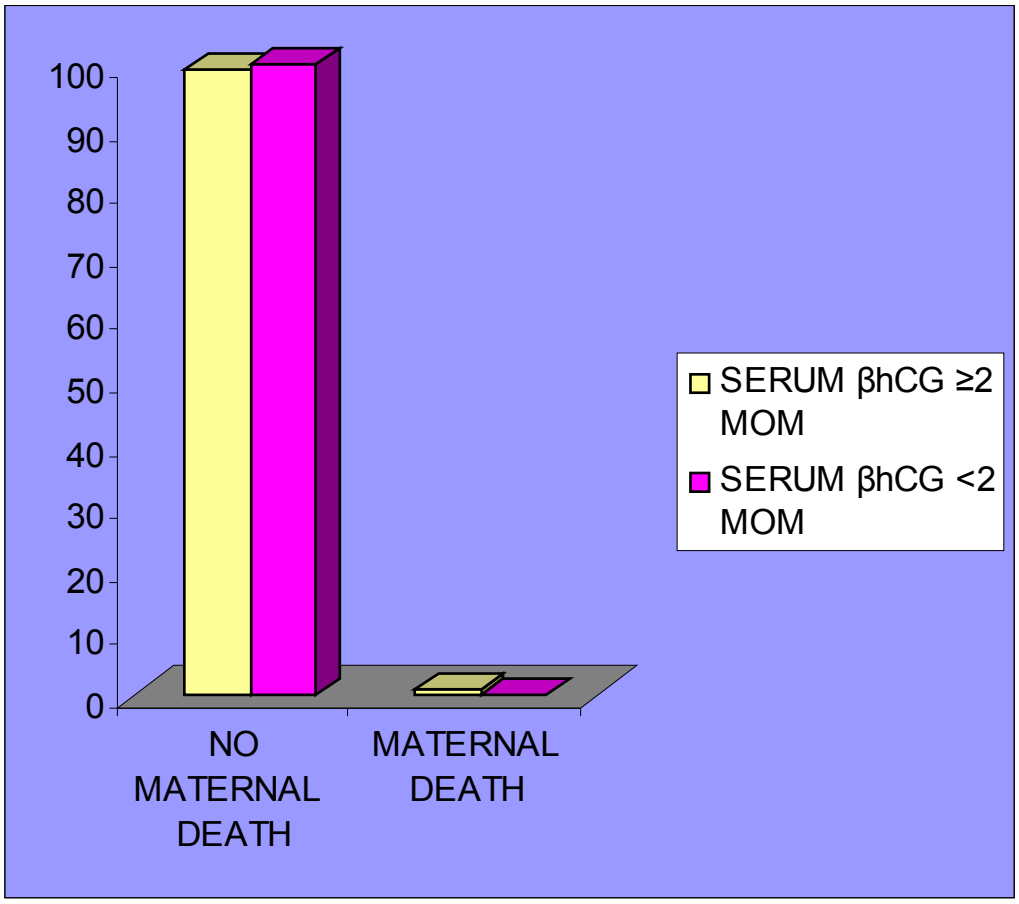
TABLE-17: COMPARISON OF MATERNAL DEATH BETWEEN THE NORMAL AND ELEVATED HCG GROUPS

MATERNAL DEATH	SERUM βhCG		TOTAL
	≥2 MOM	<2 MOM	
NO DEATH	105 (99.1%)	94 (100%)	199
MATERNAL DEATH	1 (0.9%)	0 (0.0%)	1
TOTAL	106	94	200

P = 1.00 (NOT SIGNIFICANT)

There was only one maternal death. It was in the elevated serum βhCG group.

COMPARISON OF MATERNAL DEATH BETWEEN THE NORMAL AND ELEVATED HCG GROUPS



DISCUSSION

Table 1 and 2: of the 200 patients in this study majority of women were in the age group of 20 to 25 years and 26 to 30 years. The mean age of the patients taken for this study was 25 years.

About 82.5% of women belonged to socioeconomic class v. This is an expected one as our hospital serves mainly very low income group women.

Table 3**:** Only high risk multigravidas were taken for this study. **Fawaz Alkazaleh et al.** suggested that maternal serum screening including βhCG be confined to cohorts of clinically high risk women. This view is also reinforced by a recent French study, screening 2615 unselected women with maternal serum screening and uterine artery Doppler in second trimester for adverse pregnancy outcomes including preeclampsia which concluded that this approach was of no clinical benefit in low risk patients.

Table 4 & 5 : Serum beta hCG was measured in high risk multigravidas at 15 – 20 weeks of gestation in this study.

Nathalie Lepage and David Chitayat et al., conducted a study in a group of 564 women with singleton pregnancies. They estimated serum βhCG at 15-20 weeks gestation and concluded that high maternal serum βhCG values were associated with an increased risk of adverse pregnancy outcomes including preeclampsia.

Table 6, 7 and 8 **:** In a study conducted by **Yuval Yaron et al., and Michele Cherry et al.,** it was found that patients with increased serum βhCG (≥ 2.5 MOM) were significantly at high risk of pregnancy induced hypertension with proteinuria, miscarriage, and intrauterine foetal death. They estimated maternal serum βhCG levels in 45,565 patients over a five year period (March,1991-May,1996) and compared pregnancy outcomes in patients with normal HCG and elevated HCG values.

Sorensan et al found that increased maternal serum βhCG (more than 2 MOM) was associated with significant increase in pregnancy induced hypertension (risk ratio 1.7) and proteinuric pregnancy induced hypertension (risk ratio 5.1). They suggested that hypoperfusion of placental villi leads to increased βhCG production. Such changes would also predispose to adverse outcome such as miscarriage and intrauterine foetal death.

The Ontario maternal serum screening program which was conducted to

examine the clinical significance of high maternal serum βhCG in second trimester in singleton and twin pregnancies also showed that women with singleton pregnancies having elevated serum HCG had increased adverse obstetric outcomes (22.5% severe adverse obstetric outcomes compared with only 10.9% of matched controlled population P = 0.001) including preeclampsia, antepartum haemorrhage, small for gestational age babies, preterm deliveries and miscarriages.

Benn et al reported that when maternal serum βhCG is more than 3 MOM, the incidence of preeclampsia, low birth weight babies, foetal and neonatal deaths were increased significantly.

Valiant et al., David E et al., found that there is increased incidence of preeclampsia in patients with elevated maternal serum βhCG levels at 14 – 20 weeks gestation with sensitivity of 66.7%, specificity 98%, positive predictive value of 61.4% and negative predictive value 97.3%.

The Results of this study also shows that patients with elevated maternal serum βhCG levels were associated with increased incidence of preeclampsia and other adverse obstetric outcomes. In this study the sensitivity of βhCG in predicting preeclampsia was found to be 80.85%, specificity 71.7%, positive predictive value 71.7% and negative predictive value 80.85% with diagnostic accuracy of 76%.

***Table 9 & 10*:** Patients with elevated serum βhCG had significantly earlier

deliveries (mean gestational age at delivery 38.5 weeks) compared to patients with normal βhCG values (Mean gestational age at delivery 39.54 weeks) although there was no significant difference between preterm and term deliveries.

Wenstrom et al., evaluated elevated serum βhCG values in second trimester and found that there is an increased incidence of preterm delivery and other adverse foetal and neonatal outcomes.

***Table 11*:** no difference was observed in the mode of delivery between the group of patients with normal and elevated βhCG values.

***Table 12 &13* : Liepman et al.,** reported that there is increased risk for low birth weight babies (risk ratio 4.0), preterm delivery (risk ratio 2.8), and IUGR (RR 1.8) in patients with elevated mid trimester serum βhCG values.

Morssink et al., studied the relationship between abnormal levels of maternal serum βhCG and adverse pregnancy outcomes. They found that small for gestational age babies were associated with isolated high maternal serum HCG levels (more than or equal to 2.5 MOM).

Ganapathy R, Lamont R F et al., reported that Mean Birth Weight was significantly lower in group with elevated maternal serum HCG.

Miyakoshi et al., reported that elevated levels of second trimester maternal serum hCG were as sensitive and specific in predicting SGA babies as abnormal uterine artery Doppler velocimetry .

In this study there was a signi0ficant difference in birth weight between the two HCG groups. The mean birth weight in normal HCG values was 2.800 Kg and in patients with elevated HCG values was 2.9038 Kg with a P value of 0.042.

***Table 14, 15, 16 and 17*:** **Miluensky et al** noted that elevated maternal serum HCG levels were associated with adverse foetal and neonatal outcomes.

Owen J and Boots L R reported that elevated HCG values similar to unexplained elevated maternal serum alpha feto protein are significantly associated with adverse neonatal outcomes.

Perez et al, and David et al also reported that increased incidence of adverse neonatal outcomes in patients with isolated elevation of second trimester maternal serum HCG levels and pregnancies with unexplained elevated HCG values should be regarded as high risk pregnancies and managed accordingly.

Gravett et al also concluded from his study that raised midtrimester maternal serum HCG may be an independent risk factor for subsequent adverse pregnancy outcomes.

In this study there was no significant difference observed in the 5 minute APGAR, NICU admission, Neonatal Death and maternal death in patients with elevated HCG as compared to patients with normal HCG values.

SUMMARY

- This study was conducted in 200 cases of high risk multigravid women to evaluate the validity of midtrimester serum βhCG in predicting preeclampsia.

- Majority of women in this study were in the age group of 21 – 25 years (49.5%) and of socioeconomic class v (82.5%)

- Majority of women were second gravidae (56.5%).

- The average gestational age at which serum βhCG was taken was 16 weeks.

- Of 106 cases with elevated serum βhCG (≥2 Multiples of Median), 76 cases (71.7%) developed preeclampsia. This is in contrast to 94 cases with normal HCG values, of whom 18cases (19.9%) developed preeclampsia. This is statistically significant with P value < 0.001.

- Preeclamptic patients with elevated serum βhCG values developed preeclampsia significantly earlier (average 34.97 weeks) in gestation than preeclamptic patients (36.16 weeks) with normal serum βhCG values.

- Out of 106 patients with elevated serum βhCG values 9 patients developed complications as compared to 94 patients with normal serum βhCG values of which only 2 patients developed complications.

- Patients with elevated serum βhCG values also had significantly earlier deliveries and lower birth weight babies when compared to normal serum βhCG group.

CONCLUSION

Preeclampsia is a multisystem disorder of unknown aetiology. Although many predictors have been put forth none of the methods so far described have been very much sensitive and specific to predict the development of preeclampsia. Predicting preeclampsia at an early gestational age helps us to monitor the patients closely and detect development of preeclampsia earlier and thereby reducing the maternal and perinatal mortality and morbidity. Estimating midtrimester (15 – 20 weeks) serum βhCG is a useful method in predicting preeclampsia in high risk multigravid women as it is a non invasive simple method with sensitivity of 80.85%, specificity of 71.7%, positive predictive value of 71.7% and negative predictive value of 80.85% , the diagnostic accuracy of the test is 76% (Wilson's score). The disadvantage of using serum βhCG in predicting preeclampsia is its cost and low sensitivity in nulliparous women.

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PROFORMA

Date:

Name:

Age:

IP no:

Address:

Socioeconomic status:

Booked/ un booked:

Immunised / non-immunised

Obstetric score:

LMP:

EDD:

Gestational age:

Any associated medical complications:

Previous obstetric history:

a) History of recurrent abortions (2 or more)

b) Previous history of Preeclampsia remote from term (less than 34 weeks)

c) Previous history of abruption

d) Previous history of IUGR

e) Previous history of eclampsia

f) Previous history of stillbirth

Family history:

Personal history:

Symptoms:

Clinical examination:

GENERAL EXAMINATION

a) Height

b) Weight

c) BP

d) Pedal oedema

e) Pallor +/-

CVS:

RS:

Per abdominal examination:

- Fundal height
- Foetal heart rate
- Adequacy of liquor
- presentation

INVESTIGATIONS:

- Urine - Albumin, Sugar
- Haemoglobin, PCV
- Blood – urea, sugar, creatinine
- USG :
- Serum βhCG

TREATMENT GIVEN:

GESTATIONAL AGE AT DELIVERY:

TYPE OF LABOUR - Spontaneous / induced

MODE OF DELIVERY – spontaneous vaginal delivery, caesarean section, instrumental vaginal delivery

Adverse maternal outcome – if any

Birth weight of baby: 1. ≥ 2.5 kg 2. < 2.5 Kg.

APGAR: 1. 5 minute APGAR ≥ 7 2. 5 minute APGAR < 7

3. 0 – dead born

NICU admission: YES / NO

Foetal outcome: alive / dead